

**REMARKS**

Claims 1-19 are pending in this application. Claims 3, 5-7, and 12-19 stand withdrawn. Claims 1, 2, and 4 have been amended to recite that Q<sub>3</sub> represents CHOH; *i.e.*, the 7 position of the ring is substituted by a hydroxy group. Support for this amendment can be found throughout the specification as originally filed, specifically in examples 1-1 through 1-16.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

**Rejections under 35 U.S.C. § 103(a)**

Claims 1-2, 4, and 8-11 are rejected under 35 U.S.C. 103(a) as allegedly obvious in light of the English language abstract of Japanese Patent No. JP 4178362 ("JP '362").

Specifically, the Examiner states that in view of JP '362 "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to obtain compounds within the generic disclosure of the reference, because they are structurally so similar to those claimed herein, with the reasonable expectation of achieving a successful composition, absent evidence to the contrary." Applicants respectfully disagree.

To properly determine a *prima facie* case of obviousness, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P § 2142. This is important as "impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art." *Id.* Four factual inquiries must be made: first, a determination of the scope and contents of the prior art; second, a determination of the differences between the prior art and the claims in issue; third, a determination of level of ordinary skill in the pertinent art; and fourth, an evaluation of evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success;

and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

As previously argued, the compounds of JP ‘362 differ from the claimed invention in that the urea moiety of the compounds of JP ‘362 is bound to the 1 position of the tetrahydronaphthalene in each case whereas the urea moiety of the claimed compounds is bound to the 2 position of the corresponding “A ring.”

As previously argued, Applicants respectfully submit that one of ordinary skill in the art would expect significantly different chemical properties (steric, electrochemical, pharmacological, etc) between compounds bearing a urea bound to the 1 position and compounds with a urea bound to the 2 position. Indeed, the reactivity of these two compounds is expected to be different as the substitution of different ring atoms will result in different substitution patterns. “In fused ring systems, the positions are not equivalent and there is usually a preferred orientation, even in the unsubstituted hydrocarbon” (March, *Advanced Organic Chemistry*, 6<sup>th</sup> ed. Wiley & Sons, 2007, Page 674). For Example, “naphthalene is attacked [in electrophillic aromatic substitution] primarily at the 1 position by  $\text{NO}_2^+$ ,  $\text{NH}_2^-$ , and  $\text{PH}^+$ ” (*Id.* at 676).

Furthermore, as amended, the claimed invention relates to a compound in which Q<sub>3</sub> represents CHOH. Each of the five compounds cited by the examiner are unsubstituted at this position. Furthermore, the compounds cited by the Examiner are stated to be insecticides (See cited Abstract).

As such, there are at least three points of difference between the claimed invention and the compounds cited by the Examiner. Applicants contend that one of ordinary skill in the art would have had no motivation to modify the insecticide compounds of JP ‘362 to arrive at the pharmaceutically active compounds of the claimed invention. Indeed, one of ordinary skill in the art would recognize that the differences in both substituents and substitution patterns, at a

minimum, could dramatically affect the ability of the compounds to modulate the same receptors pharmacologically.

As such, Applicants respectfully assert that one of ordinary skill in the art, at the time of the invention, would have lacked the motivation to modify the substitution position on the A ring of the instant compounds without potentially sacrificing the properties of the compounds. Similarly, Applicants respectfully assert that one of ordinary skill in the art, at the time of the invention, would have lacked the motivation to include the hydroxy substitution on the compounds of JP '362 without potentially altering the properties of the compounds therein.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103.

#### **Non- Statutory Double Patenting**

Claims 1-2, 4 and 8-11 stand provisionally rejected on the grounds of non-statutory double patenting over claims 1-16 of copending U.S. Patent Application Serial No. 10/575,027 and over claims 1-5, 7 of copending U.S. Patent Application Serial No. 10/537,217.

As it remains unknown what subject matter claimed and disclosed in the present application will be deemed allowable; any statement regarding the provisional rejection made on Applicants' part is premature. Therefore, Applicants respectfully traverse these rejections, and request that this rejection be held in abeyance until subject matter is deemed allowable in this application.

**CONCLUSION**

In view of the amendments and remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

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Respectfully submitted,

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